APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 09/847,670
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Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been indicated by the use of bold font.

In the Specification

The paragraph beginning at page 7, line 15, has been amended as follows:

In anther aspect, the present invention provides a computer-assisted method for identifying, designing , and making inhibitors of Hepatitis C virus helicase activity. Preferably the invention provides compositions, more preferably pharmaceutical compositions, including such **inhibitors[inhibotors]**.

The paragraph beginning at page 16, line 24, has been amended as follows:

The orthorhombic form of UHHO represents a conformational intermediate that is not easily modeled as a hinge, but appears as a conformation intermediate between the extreme positions of domain 2. The fact that the orthorhombic crystal form UHHO has an accessible NTP-binding site occupied by inorganic phosphate in the native crystal form suggests that it may be uniquely suited for the study of inhibitors or co-factors that bind at the NTP-binding site. This crystal form is also desirable in the study of cofactors **because[becasue]** it grows from solutions that contain significant quantities of DMSO, which is often required to bring marginally soluble chemical entities into solution with HCV helicase.

The paragraph beginning at page 24, line 5, has been amended as follows:

For example, a system for reading a data storage medium may include a computer comprising a central processing unit ("CPU"), a working memory which may be, e.g., RAM (random access memory) or "core" memory, mass storage memory (such as one or more disk drives or CD-ROM drives), one or more display devices (e.g., cathode-ray tube ("CRT") displays, light emitting diode ("LED") displays, liquid **crystal[cyrstal]** displays ("LCDs"),

electroluminescent displays, vacuum fluorescent displays, field emission displays ("FEDs"), plasma displays, projection panels, etc.), one or more user input devices (e.g., keyboards, microphones, mice, touch screens, etc.), one or more input lines, and one or more output lines, all of which are interconnected by a conventional bidirectional system bus. The system may be a stand-alone computer, or may be networked (e.g., through local area networks, wide area networks, intranets, extranets, or the internet) to other systems (e.g., computers, hosts, servers, etc.). The system may also include additional computer controlled devices such as consumer electronics and appliances.

The paragraph beginning at page 25, line 22, has been amended as follows:

The structure coordinates set forth in Tables 1, 2, or 3 can be used to aid in obtaining structural information about another crystallized molecule or molecular complex. A "molecular complex" means a protein in covalent or non-covalent association with a chemical entity or compound. The method of the invention allows determination of at least a portion of the three-dimensional structure of molecules or molecular complexes which contain one or more structural features that are similar to structural features of Hepatitis C virus helicase. These molecules are referred to herein as "structurally homologous" to Hepatitis C virus helicase. Similar structural features can include, for example, regions of amino acid identity, conserved active site or binding site motifs, and similarly arranged secondary structural elements (e.g., α helices and β sheets) and the assembly of these elements into domains. Optionally, structural homology is determined by aligning the residues of the two amino acid sequences to optimize the number of identical amino acids along the lengths of their sequences; gaps in either or both sequences are permitted in making the alignment in order to optimize the number of identical amino acids, although the amino acids in each sequence must nonetheless remain in their proper order. Preferably, two amino acid sequences are compared using the Blastp program, version 2.0.9, of the BLAST 2 search algorithm, as described by Tatusova et al., *FEMS Microbiol Lett.*, 174:247-50 (1999), and available **on the world wide web** at **[http://www.]**ncbi.nlm.nih.gov/gorf/bl2.html. Preferably, the default values for all BLAST 2

search parameters are used, including matrix = BLOSUM62; open gap penalty = 11, extension gap penalty = 1, gap x_dropoff = 50, expect = 10, wordsize = 3, and filter on. In the comparison of two amino acid sequences using the BLAST search algorithm, structural similarity is referred to as "identity." Preferably, a structurally homologous molecule is a protein that has an amino acid sequence sharing at least 65% identity with the amino acid sequence of Hepatitis C virus helicase (SEQ ID NO: 1). More preferably, a protein that is structurally homologous to Hepatitis C virus helicase includes at least one contiguous stretch of at least 50 amino acids that shares at least 80% amino acid sequence identity with the analogous portion of Hepatitis C virus helicase. Methods for generating structural information about the structurally homologous molecule or molecular complex are well-known and include, for example, molecular replacement techniques.

The paragraph beginning at page 49, line 3, has been amended as follows:

The movement of domain 2 results in a change in **the[teh]** distance separating oligonucleotide binding sites in domain 1 and domain 2. The distance between these sites is defined as the distance between the side chain oxygen of T269 and the side chain oxygen of T411 and is tabulated for each structure in Table 7.

In the Claims

For convenience, all pending claims are shown below.

31. A method for crystallizing a Hepatitis C virus helicase molecule or molecular complex comprising growing a crystal from a precipitant solution comprising purified Hepatitis C virus helicase, about 3% by weight to about 14% by weight PEG, about 5% by weight to about 15% by weight DMSO, and about 0.05M to about 0.07M potassium phosphate.

32. A method for co-crystallizing a Hepatitis C virus helicase molecule and a ligand to yield a molecular complex, comprising:

exchanging purified Hepatitis C virus helicase into a solution comprising HEPES, EDTA,